NUMERICAL MODELING OF INTERSTITIAL FLUID PRESSURE IN SOLID TUMORS: THE IMPORTANCE OF THE LYMPHATIC SYSTEM

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1. INTRODUCTION

Theoretical and experimental research showed that the interstitial fluid pressure (IFP) is elevated in solid tumors compared to normal tissue, resulting in a poor prognosis and treatment resistance. Although the lymphatic vessels are known to be partially impaired in solid tumors, the impact of the lymphatic system on IFP profiles in tumors is currently not fully understood [1]. Here, we present a 3D computational fluid dynamics (CFD) approach to study the link between the lymphatic system and the IFP in solid tumors.

2. MATERIALS AND METHODS

The interstitial fluid flow throughout the tumor is simulated in COMSOL Multiphysics (Inc., Burlington, USA) using a realistic 3D geometry of a peritoneal necrotic tumor of a mouse obtained from MRI imaging (Bruker- Infinity Lab-UGent) (Fig 1a). The interstitial flow in the tumor interstitium was described by Darcy's law and the fluid continuity equation, where the interstitial fluid source is expressed by Starling's law, and the rate of lymphatic drainage is the product of the volumetric flow rate (J_l) of lymph multiplied by the pressure difference between the IFP and the effective lymphatic pressure (p_l) [2]. The IFP at the boundary of tumor was considered to be the same as the surrounding tissue, which is 0 Pa. Four different cases were defined to investigate the impact of the lymphatics on the IFP (Fig 1c).

3. RESULTS AND DISCUSSION

The results show that even with absent lymphatic vessels, the IFP profile in the center of the tumor is noticeably changed due to the presence of a necrotic core (Fig 1b-c). Also, the presence of the necrotic core reduces the maximum IFP from 11.09 mmHg to 10.70 mmHg. Moreover, we found that a larger necrotic core reduces the IFP more profoundly.

Fig 1c shows the IFP profile in the middle of tumor (along the dashed line in Fig 1b). The presence of relatively intact lymphatic vessels heavily impacted the IFP throughout the tumor, and reduced the highest IFP value with approximately 70% when comparing the alymphatic tumor with case 1. Note that the degree of pressure drop was mainly controlled by the flow rate of lymph and by the effective lymphatic vessel pressure (Fig 1c).

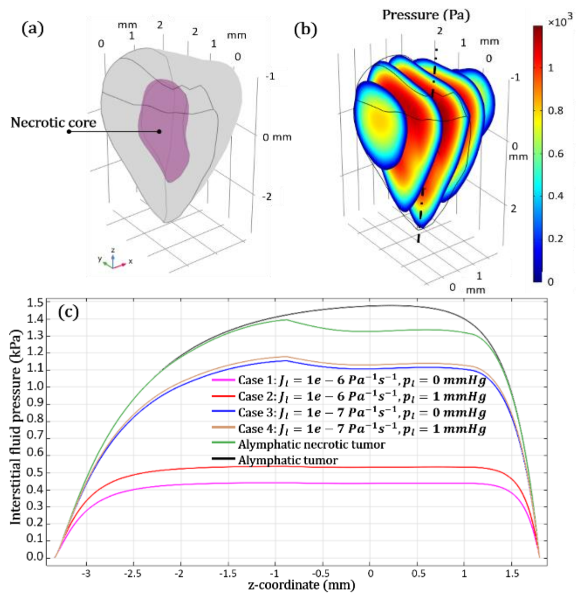

Fig 1. The impact of lymphatic drainage on IFP profile. (a) tumor geometry,(b) IFP contour of case 4 (c) and IFP profiles

In conclusion, any alteration in IFP affects the drug penetration during chemotherapy of solid tumors. Therefore, the current work highlights the importance of a comprehensive study on the properties and the extent of lymphatic system as well as the necrotic core in tumors.

References

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